

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently amended) A chemically modified ~~double stranded short interfering~~ ribonucleic acid (siRNA) molecule ~~comprising a sense strand and an antisense strand,~~ wherein:
 - a. the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides;
 - b. each strand of said siRNA nucleic acid molecule is about independently 18 to about 27 nucleotides in length; and
 - ~~b-c.~~ an 18 to 27 nucleotide sequence of the antisense strand of said siRNA nucleic acid molecule comprises about 18 to about 27 nucleotides that are is complementary to a human cholinergic receptor muscarinic 3 (CHRM3) RNA nucleotide sequence comprising SEQ ID NO:305; and the sense strand is complementary to the antisense strand; and
 - ~~e-d.~~ an 18 to 27 nucleotide sequence of the sense strand of the siRNA nucleic acid molecule is complementary to the antisense strand and comprises a portion of the CHRM3 nucleotide sequence of about an 18 to about 27 nucleotides nucleotide sequence of the human CHRM3 RNA sequence;
 - ~~d-c.~~ between about 50 and to 100 percent of the nucleotide positions nucleotides in one or both strands the sense strand and about 50 to 100 percent of the nucleotides in the antisense strand of the siRNA molecule are chemically modified with modifications independently selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications; and
 - ~~e-f.~~ the antisense strand of the siRNA molecule comprises about 5, 6, 7, 8, 9, 10 or more 2'-O-methyl nucleotides one or more of the purine nucleotides present in one or both strands of the nucleic acid molecule are 2'-O-methyl

purine nucleotides and one or more of the pyrimidine nucleotides present in one or both strands of the nucleic acid molecule are 2'-deoxy-2'-fluoro pyrimidine nucleotides.

2.-13. (Canceled)

14. (Currently amended) The ~~siRNA~~ nucleic acid molecule of claim 1, wherein ~~one~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the purine nucleotides present in the sense strand are 2'-deoxy purine nucleotides.

15. (Canceled)

16. (Currently amended) The ~~siRNA~~ nucleic acid molecule of claim 1, wherein the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends ~~of the sense strand.~~

17. (Currently amended) The ~~siRNA~~ nucleic acid molecule of claim 16, wherein said terminal cap moiety is an inverted deoxy abasic moiety.

18. (Canceled)

19. (Currently amended) The ~~siRNA~~ nucleic acid molecule of claim 1, wherein ~~one~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the purine nucleotides present in the antisense strand are 2'-O-methyl purine nucleotides.

20. (Currently amended) The ~~siRNA~~ nucleic acid molecule of claim 1, wherein ~~one~~ 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the purine nucleotides present in said antisense strand are 2'-deoxy[[-]] purine nucleotides.

21. (Currently amended) The ~~siRNA~~ nucleic acid molecule of claim 1, wherein the antisense strand ~~comprises~~ includes a terminal phosphorothioate internucleotide linkage at the 3' end ~~of said antisense strand.~~

22.-29. (Canceled)

30. (Currently amended) The ~~siRNA~~ nucleic acid molecule of claim 1, wherein the 5'-end of the antisense strand includes a terminal phosphate group.

31. (Currently amended) A composition comprising the ~~siRNA~~ nucleic acid molecule of claim 1 in a pharmaceutically acceptable carrier or diluent.
32. (New) The nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the pyrimidine nucleotides present in the sense strand are 2'-O-methyl pyrimidine nucleotides.
33. (New) The nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the pyrimidine nucleotides present in the sense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
34. (New) The nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
35. (New) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule comprises one or more ribonucleotides.
36. (New) The nucleic acid molecule of claim 1, wherein 1, 2, or 3 of the purine nucleotides present in the sense strand are 2'-O-methyl purine nucleotides.
37. (New) The nucleic acid molecule of claim 1, wherein the antisense strand, sense strand, or both the antisense strand and sense strand include a 3'-overhang of 1-3 nucleotides.
38. (New) The nucleic acid molecule of claim 37, wherein the nucleotides of the 3'-overhang are chemically modified to comprise one or more phosphorothioate internucleotide linkages, 2'-O-methyl ribonucleotides, 2'-deoxy-2'-fluoro ribonucleotides, 2'-deoxy ribonucleotides, universal base nucleotides, 5-C-methyl nucleotides, inverted deoxybasic moieties or a combination thereof.
39. (New) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule further includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more phosphorothioate internucleotide linkages in the sense strand, the antisense strand, or both the sense strand and the antisense strand.
40. (New) The nucleic acid molecule of claim 1, wherein said nucleic acid molecule further includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more 2'-O-methoxyethyl (MOE) nucleotides in the sense strand, the antisense strand, or both the sense strand and the antisense strand.

41. (New) the nucleic acid molecule of claim 1, wherein said nucleic acid molecule further includes 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more locked nucleic acid (LNA) nucleotides in the sense strand, the antisense strand, or both the sense strand and the antisense strand.
42. (New) A chemically modified nucleic acid molecule comprising a sense strand and a separate antisense strand, wherein:
- a) each strand of said nucleic acid molecule is independently 18 to 27 nucleotides in length;
 - b) an 18 to 27 nucleotide sequence of the antisense strand of said nucleic acid molecule is complementary to a human CHRM3 RNA sequence comprising SEQ ID NO:305;
 - c) an 18 to 27 nucleotide sequence of the sense strand of said nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human CHRM3 RNA sequence;
 - d) the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both of the 5' and 3' ends;
 - e) one or more of the nucleotides present in the sense strand and one or more of the nucleotides present in the antisense strand are 2'-O-methyl modified nucleotides; and
 - f) one to ten or more of the pyrimidine nucleotides present in the sense strand and one to ten or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides.
43. (New) A composition comprising the nucleic acid molecule of claim 42 in a pharmaceutically acceptable carrier or diluent.
44. (New) A chemically modified nucleic acid molecule, wherein:

- a) the nucleic acid molecule comprises a sense strand and a separate antisense strand, each strand having one or more pyrimidine nucleotides and one or more purine nucleotides;
 - b) each strand of the nucleic acid molecule is independently 18 to 27 nucleotides in length;
 - c) an 18 to 27 nucleotide sequence of the antisense strand of the nucleic acid molecule is complementary to a human CHRM3 RNA sequence comprising SEQ ID NO:305;
 - d) an 18 to 27 nucleotide sequence of the sense strand of the nucleic acid molecule is complementary to the antisense strand and comprises an 18 to 27 nucleotide sequence of the human CHRM3 RNA sequence;
 - e) at least 50% of the nucleotides of each strand of said nucleic acid molecule comprise modified nucleotides having a sugar modification selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, and deoxybasic modifications;
 - f) at least one of said sugar modifications is a 2'-O-methyl modification; and
 - g) each strand of said nucleic acid molecule has no more than 3 consecutive ribonucleotides.
45. (New) A composition comprising the nucleic acid molecule of claim 44, in a pharmaceutically acceptable carrier or diluent.
46. (New) A method of modulating the expression of human CHRM3 gene in a cell, comprising administering the chemically modified nucleic acid molecule of claim 1 to the cell under conditions suitable for modulating the expression of human CHRM3 gene in the cell.
47. (New) A method of modulating the expression of human CHRM3 gene in a cell, comprising administering the chemically modified nucleic acid molecule of claim 44 to the cell under conditions suitable for modulating the expression of human CHRM3 gene in the cell.